

Please add the following claims:

--64. A method for producing biologically active human fibrinogen that is converted to fibrin upon reaction with human thrombin comprising:

C1 providing a first DNA segment encoding a secretion signal operably linked to a heterologous fibrinogen A α chain, a second DNA segment encoding a secretion signal operably linked to a heterologous fibrinogen B β chain, and a third DNA segment encoding a secretion signal operably linked to a heterologous fibrinogen γ chain, wherein each chain is from the same species, and wherein each of said first, second and third segments is operably linked to additional DNA segments required for its expression in the mammary gland of a host female mammal;

introducing said DNA segments into a fertilized egg of a non-human mammalian species heterologous to the species of origin of said fibrinogen chains;

inserting said egg into an oviduct or uterus of a female of said mammalian species to obtain offspring carrying said DNA segments;

breeding said offspring to produce female progeny that express said first, second and third DNA segments and produce milk containing biologically active human fibrinogen that is converted to fibrin upon reaction with human thrombin encoded by said segments;

collecting milk from said female progeny; and

recovering the biologically active human fibrinogen that is converted to fibrin upon reaction with human thrombin from the milk.

65. A transgenic non-human female mammal that produces recoverable amounts of biologically active human fibrinogen that is converted to fibrin upon reaction with human thrombin in its milk, wherein said mammal comprises:

a first DNA segment encoding a secretion signal operably linked to a heterologous fibrinogen A α chain,

a second DNA segment encoding a secretion signal operably linked to a heterologous fibrinogen B β chain, and

a third DNA segment encoding a secretion signal operably linked to a heterologous fibrinogen γ chain, and further wherein each chain is derived from the same species and is operably linked to additional DNA segments required for its expression in the mammary gland of a host female mammal.

66. A method for producing biocompetent fibrinogen comprising:

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providing a transgenic female non-human mammal carrying in its germline heterologous DNA segments encoding $A\alpha$, $B\beta$, and γ chains of fibrinogen, wherein said segments are expressed in a mammary gland of said mammal and biocompetent fibrinogen encoded by said segments is secreted into milk of said mammal;

collecting milk from said mammal; and

recovering said biocompetent fibrinogen from said milk.

67. The method of claim 66, wherein said transgenic non-human female mammal is selected from the group consisting of a rodent, rabbit, pig, sheep, goat, and cattle.

68. The method of claim 66, wherein said mammal is a sheep.

69. A non-human mammal carrying in its germline DNA segments encoding $A\alpha$, $B\beta$, and γ chains of fibrinogen, wherein female progeny of said mammal express said DNA segments in a mammary gland to produce biocompetent fibrinogen.

70. The mammal of claim 69, which is selected from the group consisting of rodent, rabbit, pig, sheep, goat, and cattle.

71. The mammal of claim 69 which is a female.

72. The mammal of claim 69 which is a male.

73. The mammal of claim 69, which is a sheep.

74. A method for producing biocompetent fibrinogen comprising:

providing a first DNA segment encoding a heterologous fibrinogen A α chain, a second DNA segment encoding a heterologous fibrinogen B β chain; and a third DNA segment encoding a heterologous fibrinogen γ chain, wherein each chain is from the same species, and wherein each of said first, second and third segments is operably linked to additional DNA segments required for its expression in the mammary gland of a host female mammal;

introducing said DNA segments into a fertilized egg of a non-human mammalian species heterologous to the species of origin of said fibrinogen chains;

inserting said egg into an oviduct or uterus of a female of said mammalian species to obtain offspring carrying said DNA segments;

breeding said offspring to produce female progeny that express said first, second and third DNA segments and produce milk containing biocompetent fibrinogen encoded by said segments;

collecting milk from said female progeny; and
recovering the biocompetent fibrinogen from the milk.

75. A method according to claim 74, wherein said species into which said DNA segments are introduced is selected from the group consisting of a rodent, rabbit, sheep, pig, goat and cattle.

76. A method according to claim 74, wherein said first, second, and third DNA segments comprises an intron.

77. A method according to claim 74, wherein each of said first, second and third DNA segments is operably linked to a transcription promoter selected from the group consisting of casein, β -lactoglobulin, α -lactalbumin and whey acidic protein gene promoters.

78. A method according to claim 74, wherein said first, second and third DNA segments are expressed under the control of a β -lactoglobulin promoter.

79. A method according to claim 74, wherein said introducing step comprises injecting said first, second and third DNA segments into a pronucleus of said fertilized egg.

80. A method according to claim 74, wherein said fibrinogen is human fibrinogen.

81. A method according to claim 74, wherein said species into which said DNA segments is introduced is sheep.

82. A method of producing biocompetent fibrinogen comprising:

incorporating a first DNA segment encoding an A α chain of fibrinogen into a β -lactoglobulin gene to produce a first gene fusion comprising a β -lactoglobulin promoter operably linked to the first DNA segment;

incorporating a second DNA segment encoding an B β chain of fibrinogen into a β -lactoglobulin gene to produce a second gene fusion comprising a β -lactoglobulin promoter operably linked to the second DNA segment;

incorporating a third DNA segment encoding a γ chain of fibrinogen into a β -lactoglobulin gene to produce a third gene fusion comprising a β -lactoglobulin promoter operably linked to the third DNA segment, wherein each of said first, second and third segments are of the same species;

introducing said first, second and third gene fusions into the germ line of a non-human mammal so that said DNA segments are expressed in a mammary gland of said mammal or its female progeny and biocompetent fibrinogen is secreted into milk of said mammal or its female progeny;

obtaining milk from said mammal or its female progeny; and recovering said biocompetent fibrinogen from said milk.

83. A method according to claim 82, wherein said mammal is selected from the group consisting of a rodent, rabbit, sheep, pig, goat or cow.

84. A method according to claim 82, wherein each of said first, second and third gene fusions comprises an intron.

85. A method according to claim 82, wherein said introducing step comprises injecting said first, second and third gene fusions into a pronucleus of a fertilized egg and inserting said egg into an oviduct of a pseudopregnant female to produce female offspring carrying said gene fusions into the germ line, wherein said egg and said pseudopregnant female are of the same species.

86. The method of claim 82, wherein said mammal is a sheep.

87. A transgenic non-human female mammal that produces recoverable amounts of biocompetent human fibrinogen in its milk, wherein said mammal comprises:

a first DNA segment encoding a heterologous fibrinogen A α chain,

a second DNA segment encoding a heterologous fibrinogen B β chain,

a third DNA segment encoding a heterologous fibrinogen γ chain, and

further wherein each chain is derived from the same species and is operably linked to additional DNA segments required for its expression in the mammary gland of a host female mammal.

88. The mammal according to claim 87 which is a sheep.

89. A process for producing a transgenic offspring of a mammal comprising:

providing a first DNA segment encoding a first DNA encoding a heterologous fibrinogen A α chain, a second DNA segment encoding a second DNA encoding a heterologous fibrinogen B β chain, and a third DNA segment encoding a third DNA encoding a heterologous fibrinogen γ chain, wherein each chain is derived from the same species, and wherein each of said first, second and third segments is operably linked to additional DNA segments required for its expression in a mammary gland of a host female mammal;

introducing said DNA segments into a fertilized egg of a non-human species heterologous to the species of origin of said fibrinogen chains;

inserting said fertilized egg into an oviduct or uterus of a female of said mammalian species; and

allowing said fertilized egg to develop thereby producing transgenic offspring carrying said first, second and third DNA segments, wherein female progeny of said mammal express said DNA segments in a mammary gland to produce biocompetent fibrinogen.

90. A process according to claim 89, wherein said offspring is female.

91. A process according to claim 89, wherein said offspring is male.

92. A non-human mammal produced according to the process of claim 89.

93. A non-human mammal produced according to claim 92, wherein said mammal is female.

94. A non-human mammal according to claim 93 that produces milk containing biocompetent fibrinogen encoded by said DNA segments.

95. A non-human mammal according to claim 92, wherein said mammal is a male. --